

## **RESPONSE**

### **I. Election/Restriction Requirement**

In spite of the Examiner's previous instance that the original claims were directed to more than one invention, the Examiner has chosen to rejoin all the claims in the present case. The Applicants acknowledge and welcome this action.

### **II. Status of the Claims**

Claims 2-4 have been cancelled entirely without prejudice and without disclaimer. New claims 5-18 have been added to better claim the present invention. As a result, claims 1, and 5-18 are therefore pending in the present case.

### **III. Support for the Claims**

New claim 5 has been added to more clearly claim aspects of the invention. Claim 5 finds support throughout the specification and sequence listing as originally filed, with particular support being found in original claim 1 on which it depends and on original SEQ ID NO: 1.

New claim 6 has been added to more clearly claim aspects of the invention. Claim 6 finds support throughout the specification and sequence listing as originally filed, with particular support being found in original claim 1 on which it depends and on original SEQ ID NO: 3.

New claim 7 has been added to more clearly claim aspects of the invention. Claim 7 finds support throughout the specification and sequence listing as originally filed, with particular support being found in original claim 1 on which it depends and on original SEQ ID NO: 5.

New claim 8 has been added to more clearly claim aspects of the invention. Claim 8 finds support throughout the specification and sequence listing as originally filed, with particular support being found in original claim 1 on which it depends and in original SEQ ID NO: 7.

New claim 9 has been added to better claim aspects of the invention. Claim 9 finds support throughout the specification, in claim 1 and sequence listing as originally filed, with particular support being found at least at page 15, lines 1-7 and in SEQ ID NOS: 2, 4, 6 and 8.

New claims 10-13 have been added to better and more clearly claim aspects of the invention. Claims 10-13 are dependent upon new claim 9, which finds support throughout the specification, in claim

1 and sequence listing as originally filed, with particular support being found at least at page 15, lines 1-7. In addition new claims 8-13 also find particular support in SEQ ID NOS: 1, 3, 5, and 7, respectively.

New claim 14 has been added to more clearly claim aspects of the invention. Claim 14 finds support throughout the specification, claims and sequence listing as originally filed, with particular support being found at least on page 15, lines 7-18.

New claims 15-18 have been added to better and more clearly claim aspects of the invention. Claims 15-18 are dependent upon new claim 14, which finds support throughout the specification, in claim 1 and sequence listing as originally filed, with particular support being found at least at page 15, lines 7-18. In addition new claims 15-18 also find particular support in SEQ ID NOS: 1, 3, 5, and 7, respectively.

As new claims 5-18 are fully supported by the specification, sequence listing and claims as originally filed, they do not constitute new matter and entry is therefore respectfully requested.

#### **IV. Rejection of Claims Under 35 U.S.C. § 101**

The Action rejects claims under 35 U.S.C. § 101, allegedly because the claimed invention lacks support by either a specific and substantial asserted utility or a well established utility.

The Action rejects all claims under 35 U.S.C. § 101, as allegedly lacking a patentable utility due to not being supported by a specific, substantial, and credible utility or, in the alternative, a well-established utility. Because the present application describes novel variants of human metalloprotease ADAM19, a molecule whose activity and utility are well-known to the art, Applicants respectfully traverse.

Applicants respectfully submit that the legal test for utility involves an assessment of whether those skilled in the art would find any of the utilities described for the invention to be credible or believable. According to the Examination Guidelines for the Utility Requirement, if the applicant has asserted that the claimed invention is useful for any particular purpose (i.e., it has a “specific and substantial utility”) and the assertion would be considered credible by a person of ordinary skill in the art, the Examiner should not impose a rejection based on lack of utility (66 Federal Register 1098, January 5, 2001).

In *In re Brana*, (34 USPQ2d 1436 (Fed. Cir. 1995), “*Brana*”), the Federal Circuit admonished the P.T.O. for confusing “the requirements under the law for obtaining a patent with the requirements for obtaining government approval to market a particular drug for human consumption”.

*Brana* at 1442. The Federal Circuit went on to state:

At issue in this case is an important question of the legal constraints on patent office examination practice and policy. The question is, with regard to pharmaceutical inventions, what must the applicant provide regarding the practical utility or usefulness of the invention for which patent protection is sought. This is not a new issue; it is one which we would have thought had been settled by case law years ago.

*Brana* at 1439, emphasis added. The choice of the phrase “utility or usefulness” in the foregoing quotation is highly pertinent. The Federal Circuit is evidently using “utility” to refer to rejections under 35 U.S.C. § 101, and is using “usefulness” to refer to rejections under 35 U.S.C. § 112, first paragraph. This is made evident in the continuing text in *Brana*, which explains the correlation between 35 U.S.C. §§ 101 and 112, first paragraph. The Federal Circuit concluded:

FDA approval, however, is not a prerequisite for finding a compound useful within the meaning of the patent laws. Usefulness in patent law, and in particular in the context of pharmaceutical inventions, necessarily includes the expectation of further research and development. The stage at which an invention in this field becomes useful is well before it is ready to be administered to humans. Were we to require Phase II testing in order to prove utility, the associated costs would prevent many companies from obtaining patent protection on promising new inventions, thereby eliminating an incentive to pursue, through research and development, potential cures in many crucial areas such as the treatment of cancer.

*Brana* at 1442-1443, citations omitted. In assessing the question of whether undue experimentation would be required in order to practice the claimed invention, the key term is “undue”, not “experimentation”. *In re Angstadt and Griffin*, 190 USPQ 214 (C.C.P.A. 1976). The need for some experimentation does not render the claimed invention unpatentable. Indeed, a considerable amount of experimentation may be permissible if such experimentation is routinely practiced in the art. *In re Angstadt and Griffin, supra*; *Amgen, Inc. v. Chugai Pharmaceutical Co., Ltd.*, 18 USPQ2d 1016 (Fed. Cir. 1991). As a matter of law, it is well settled that a patent need not disclose what is well known in the art. *In re Wands*, 8 USPQ 2d 1400 (Fed. Cir. 1988).

Even under the newly installed utility guidelines, Applicants note that MPEP 2107 (II)(B)(1) states:

(1) If the applicant has asserted that the claimed invention is useful for any particular practical purpose (i.e., it has a “specific and substantial utility”) and the assertion would be considered credible by a person of ordinary skill in the art, do not impose a rejection based on lack of utility. (MPEP 2107 (II)(B)(1))

Applicants would first like to invite the Examiner’s attention to the fact that a sequence sharing greater than 98% identity at the amino acid level (956/963) with SEQ ID NO:2 of the present invention is present in the leading scientific repository for biological sequence data (GenBank), and has been annotated by third party scientists *wholly unaffiliated with Applicants* as “metalloprotease-disintegrin meltrin beta [*Homo sapiens*] (GenBank accession number AAG50282, alignment and information provided as **Exhibit A**). Applicants note that metalloprotease-disintegrin meltrin beta is also known to the art as ADAM 19. SEQ ID NO:2 identifies a slightly longer isoform, which is clearly encoded by the same genetic locus. Clearly those of skill in the art have identified the sequence of SEQ ID NO:2 as encoding a human metalloprotease, in particular ADAM19. This clearly supports Applicant’s assertion that those of skill in the art would recognize the present invention as a metalloprotease, variants of ADAM 19 in particular.

The function of ADAM19 is very well known to those of skill in the art, as exemplified by many scientific publications, for example: “Catalytic properties of ADAM19” (Chesneau, *et al.*, J Biol Chem. **278**(25):22331-22340:2003: **Exhibit B**); “Inverse regulation of the ADAM-family members, decysin and MADDAM/ADAM19 during monocyte differentiation” (Fritsche *et al.*, Immunology **110**(4):450-457, 2003: abstract provided as **Exhibit C**); “Essential role for ADAM19 in cardiovascular morphogenesis” (Zhou, *et al.*, Mol Cell Biol. **24**(1):96-104, 2003: abstract provided as **Exhibit D**) and “Essential role for Meltrin beta (ADAM19) in heart development” (Kurohara, *et al.*, Dev Biol. **267**(1):14-28, 2004: abstract provided as **Exhibit E**). Therefore, clearly, there can be no question that the sequences of the present invention encode molecules (ADAM 19 variants) that have a specific, substantial and well established utility.

The legal test for utility simply involves an assessment of whether those skilled in the art would find any of the utilities described for the invention to be credible or believable. Given this GenBank annotation and the described publications, there can be no question that those skilled in the art would clearly believe that the molecule encoded by the sequences of the present invention have specific,

substantial and well established utility. As such, the scientific evidence clearly establishes that Applicants have described an invention whose utility is in full compliance with the provisions of 35 U.S.C. § 101, and therefore Applicants respectfully request withdrawal of the rejection.

The Action suggests that Applicants could not have made an assertion regarding utility as there are no working examples, indicating a need for such information are misplaced. It has long been established that "there is no statutory requirement for the disclosure of a specific example". *In re Gay*, 135 USPQ 311 (C.C.P.A. 1962). In the specification, Applicants asserted that the sequences of the present invention share sequence similarity with mammalian meltrin-beta\ADAM 19 homologue metalloproteases (page 1, lines 11-12) and that the sequences of the present invention encode a protein that shares structural similarity particularly with metalloproteases and disintegrins such as meltrin-beta and ADAM 19 (on page 2, lines 1-4). Applicants respectfully submit that those of skill in the art would recognize these statements as an assertion that the sequences of the present invention do indeed encode metalloproteases like ADAM 19. Applicants' assertion is that the sequences of the present invention encode novel variants of ADAM 19. As novel variants these sequences differ slightly from previously identified sequences encoding ADAM 19, but certainly as expected, share structural similarity with sequences known to encode ADAM 19. These statements in the specification assert that the sequences of the present invention and ADAM 19 share a similarity in structure, a similarity in function and a similarity in biological function. This would be accepted by those of skill in the art, as it is generally recognized that there is a structure-function relationship. Absent any evidence of record that the described ADAM19 variants somehow fail to function as does ADAM 19, the Examiner has failed to meet his/her burden of establishing that the Applicants' assertion of protein function is not credible. Accordingly, the Examiner is respectfully requested to either provide evidence that substantially and specifically refutes the Applicants' asserted function/utility, or withdraw the rejection. Clearly, the sequences of the present invention have patentable utility and pending rejections under 35 U.S.C. § 101 and 35 U.S.C. § 112, first paragraph should be withdrawn.

If, somehow, the above arguments were not deemed sufficient, it should also be noted that the rejection of the present invention due to lack of patentable utility also runs contrary to Example 10 of the PTO's Revised Interim Utility Guidelines Training Materials (pages 53-55), which establishes that a rejection under 35 U.S.C. § 101 as allegedly lacking a patentable utility and under 35 U.S.C. § 112, first paragraph as allegedly unusable by the skilled artisan due to the alleged lack of patentable utility,

is not proper when there is no reason to doubt the asserted utility of a full length sequence that has a similarity score of 95% to a protein having a known function. In the Analysis portion of Example 10 it states that “Based on applicant’s disclosure and the results of the PTO search, there is no reason to doubt the assertion that SEQ ID NO:2 encodes a DNA ligase. Further DNA ligases have a well-established use in the molecular biology art based on this class of proteins ability to ligate DNA. ....Note that if there is a well-established utility already associated with the claimed invention, the utility need not be asserted in the specification as filed..... Thus the conclusion reached from this analysis is that a 35 U.S.C. § 101 and a 35 U.S.C. § 112 first paragraph, utility rejection should not be made.”

In the present case, clearly evidence supports Applicants’ assertions that the sequences of the present invention encode novel variants of ADAM19, a class of proteins for which there is a well established utility that is recognized by those of skill in the art. The present case is identical to that presented in Example 10 of the Revised Interim Utility Guidelines Training Materials (pages 53-55). In the present case it is clear that the sequences of the present invention encode novel variants of ADAM19 with greater than a 95% identity to a protein having a known function (ADAM19), as asserted in the specification. However, even if, *arguendo*, Applicants had failed to assert this utility, according to the guidelines “Note that if there is a well-established utility already associated with the claimed invention, the utility need not be asserted in the specification as filed... Thus the conclusion reached from this analysis is that a 35 U.S.C. § 101 and a 35 U.S.C. § 112 first paragraph, utility rejection should not be made”(emphasis added). Thus, the present rejection of the presently claimed invention under a 35 U.S.C. § 101 and a 35 U.S.C. § 112 first paragraph utility rejection should not have been made and should be withdrawn.

In addition to the above presented evidence countering the Actions suggestion that Applicants knew of no specific use at the time the application was filed that would permit an immediate use by the public of a disclosed nucleic acid sequence. However, the specification details a number of uses for the presently claimed polynucleotide sequences, among these were, use in diagnostic assays such as forensic analysis (see, for example, the specification at page 3, line 12 and page 12, line 13), identification of protein coding sequence and identification of exon splice junctions (see, for example, the specification at page 5, line 5, and page 11, lines 31-33), in mapping the sequences to a specific region of a human chromosome (see, for example, the specification at page 3, lines 2-6), and in

assessing gene expression patterns, particularly using a high throughput “chip” format (see, for example, the specification at page 6, line 15 through page 8).

In the Action the position that the argument that the polymorphisms described in the specification (on page 17, lines 19-27) have patentable utility is also deemed to be non-persuasive. This is allegedly because the asserted utilities of the present nucleic acid sequences and their identified polymorphisms in forensic analysis, human population biology, or paternity identification are not specific or substantial.

Naturally occurring genetic polymorphisms such as those described in the present specification are both the basis of, and critical to, *inter alia*, forensic genetic analysis and genetic analysis intended to resolve issues of identity and paternity. Therefore, Applicants find this position difficult to comprehend, given that the results of identity and paternal analysis often have great emotional and substantial economic impact. This does not sound like a throw away utility, rather it sounds like a very substantial and real world utility. What could be more substantial and real world than the loss of an individual’s freedom through incarceration and in some cases even the loss of life through execution? Yet forensic analysis based on identified polymorphisms is often used to convict or acquit in many cases. Both paternal and forensic genetic analysis is based on the use of identified polymorphisms. This is a well known and generally accepted by those of skill in the art, who would readily recognize the utility and value of any identified polymorphism. Without identified polymorphisms, one would not be able to carry out such forensic or paternal analyses. The present application has identified just such essential polymorphisms within the sequences of the present invention which identify variants of the human metalloprotease, ADAM 19.

As such polymorphisms are the basis for forensic analysis, paternity identification and population biology studies, which are undoubtedly “real world” utilities, the present sequences must in themselves be useful. In and of themselves each of these polymorphisms, including the silent ones, has significant and specific utility, the specificity of this utility is only amplified by the presence of so many polymorphisms that can arise in various combinations. It is also important to note that the presence of more useful polymorphic markers for such analysis would not mean that the present sequences lack utility.

Applicants respectfully point out that those of skill in the art would readily recognize that the presently described polymorphisms, exactly as they were described in the specification as originally

filed, are useful in forensic analysis, population biology and paternity analysis to specifically identify individual members of the human population based on the presence or absence of the described polymorphism. Simply because the use of these polymorphic markers will necessarily provide additional information on the percentage of particular subpopulations that contain one or more of these polymorphic markers does not mean that “additional research” is needed in order for these markers as they are presently described in the instant specification to be of use to forensic science. Without further experimentation those of skill in the art would recognize the utility of the identified polymorphisms and how the asserted markers can distinguish 50% of the population in the worst case scenario. Thus the presence or the absence of a particular specific polymorphism is sufficient for use in the proposed utilities. Applicants provide the following detailed explanation. Those of skill in the art would recognize that in the worst case, least useful situation, a marker would be present in half of a population and absent from the other half. Therefore the probability of an individual having such a marker would be 1 in 2 or 50%. Using the forensic analysis scenario for example, the analysis will have removed 50% of the possible suspects from the list, as either the suspect has the identified polymorphism or not. However, if a polymorphism were present in only say 10% of the population, the probability of an individual having such a polymorphic marker would be 1 in 10 (10%) and 90% of suspects could be eliminated from investigation or prosecution based on the presence or absence of the polymorphism. Clearly eliminating 90% of the suspects is better than eliminating 50% of the suspects. That said, eliminating 50% or half of the suspects on a list is without question very useful to any investigator. To reiterate, using the polymorphic markers as described in the specification as originally filed will definitely distinguish members of a population from one another. In the worst case scenario, each of these markers are useful to distinguish 50% of the population (in other words, the marker being present in half of the population). The ability to eliminate 50% of the population from a forensic analysis clearly is a real world, practical utility. Therefore, any allegation that the use of the presently described polymorphic markers is only potentially useful would be completely without merit, and would not support the alleged lack of utility.

Perhaps the Examiner is assuming that since any human nucleic acid sequence that contains a naturally occurring polymorphism can be used in forensic analysis, in human paternity determinations or human population migration determinations, such utilities are generic and therefore lack substantial and specific utility. First, Applicants submit that until a specific polymorphic marker is actually



described it has very limited utility in forensic analysis. Put another way, simply because there is a possibility, even a significant likelihood, that a particular nucleic acid sequence will contain a polymorphism and thus be useful in forensic analysis, until such a specific polymorphism is actually identified and described, such a likelihood is meaningless. The present case contains identified polymorphisms that occur in novel variants of the human metalloprotease ADAM 19. The Examiner is perhaps attempting to use the information presented for the first time by Applicants in the instant specification as hindsight verification that the presently claimed sequence would be expected to have polymorphic markers. Such a hindsight analysis based on Applicants discovery would not be proper.

Alternatively, the assumption that since any sequence containing a naturally occurring polymorphism can be used such utilities are generic and therefore lack substantial and specific utility may represent a confusion between the requirement for a specific utility, which is the proper standard for utility under 35 U.S.C. § 101, with a requirement for a unique utility. The relevant case law cited by Applicants makes it abundantly clear that the presence of other or even more useful polymorphic markers for forensic analysis does **not** mean that the present sequences lack a specific utility. As clearly stated by the Federal Circuit in *Carl Zeiss Stiftung v. Renishaw PLC*, 20 USPQ2d 1101 (Fed. Cir. 1991; “*Carl Zeiss*”):

An invention need not be the best or only way to accomplish a certain result, and it need only be useful to some extent and in certain applications: “[T]he fact that an invention has only limited utility and is only operable in certain applications is not grounds for finding a lack of utility.” *Envirotech Corp. v. Al George, Inc.*, 221 USPQ 473, 480 (Fed. Cir. 1984)

Importantly, the holding in the *Carl Zeiss* case is mandatory legal authority that essentially controls the outcome of the present appeal. This case, and particularly the cited quote, directly rebuts any such argument. Furthermore, the requirement for a unique utility is clearly not the standard adopted by the Patent and Trademark Office. If every invention were required to have a unique utility, the Patent and Trademark Office would no longer be issuing patents on batteries, automobile tires, golf balls, golf clubs, and treatments for a variety of human diseases, such as cancer and bacterial or viral infections, just to name a few particular examples, because examples of each of these have already been described and patented. All batteries have the exact same utility - specifically, to provide power. All automobile

tires have the exact same utility - specifically, for use on automobiles. All golf balls and golf clubs have the exact same utility - specifically, use in the game of golf. All cancer treatments have the exact same utility - specifically, to treat cancer. All anti-infectious agents have the exact same broader utility - specifically, to treat infections. However, only the briefest perusal of virtually any issue of the Official Gazette provides numerous examples of patents being granted on each of the above compositions every week. Furthermore, if a composition needed to be unique to be patented, the entire class and subclass system would be an effort in futility, as the class and subclass system serves solely to group such common inventions, which would not be required if each invention needed to have a unique utility. Thus, the present sequence clearly meets the requirements of 35 U.S.C. § 101.

Although the above discussions are believed to be dispositive of the utility issue in this case, Applicants would like to further direct the Examiner's attention to the parts of the specification that describe the use of sequences in a gene chip format to provide a high throughput analysis of the relevant cellular "transcriptome", including assessing temporal and tissue specific gene expression patterns, particularly using a high throughput "chip" format (specification at or about page 6, line 15 through page 8).

Evidence of the "real world" substantial utility of the present invention is further provided by the fact that there is an entire industry established based on the use of gene sequences or fragments thereof in a gene chip format. Perhaps the most notable gene chip company is Affymetrix. However, there are many companies which have, at one time or another, concentrated on the use of gene sequences or fragments, in gene chip and non-gene chip formats, for example: Gene Logic, ABI-Perkin-Elmer, HySeq and Incyte. In addition, one such company, Rosetta Inpharmatics, was viewed to have such "real world" value that it was acquired by large pharmaceutical company, Merck & Co., for substantial sums of money (net equity value of the transaction was \$620 million). The "real world" substantial industrial utility of gene sequences or fragments would, therefore, appear to be widespread and well established. Clearly, persons of skill in the art, as well as venture capitalists and investors, readily recognize the utility, both scientific and commercial, of genomic data in general, and specifically human genomic data. Billions of dollars have been invested in the human genome project, resulting in useful genomic data (see, *e.g.*, Venter *et al.*, 2001, Science 291:1304, presented as **Exhibit F**). The results have been a stunning success as the utility of human genomic data has been widely recognized as a great gift to humanity (see, *e.g.*, Jasny and Kennedy, 2001, Science 291:1153, presented as **Exhibit G**).

Clearly, the usefulness of human genomic data, such as the presently claimed nucleic acid molecules, is substantial and credible (worthy of billions of dollars and the creation of numerous companies focused on such information) and well-established (the utility of human genomic information has been clearly understood for many years). The sequences of the present invention have particularly specific utility in DNA gene chip based analysis as they have been identified to contain several coding region single nucleotide polymorphisms (cSNPs), thus increasing their utility in DNA gene chip based analysis.

DNA chips clearly have utility, as evidenced by hundreds of issued U.S. Patents, as exemplified by U.S. Patent Nos. 5,445,934, 5,556,752, 5,744,305, 5,837,832, 6,156,501 and 6,261,776 (Exhibits H-M; copies of issued U.S. Patents not provided pursuant to current United States Patent and Trademark Office policy). Accordingly, the present sequence has a specific utility in such DNA chip applications. Clearly, compositions that enhance the utility of such DNA chips, like the present sequences, which encode variants of the human metalloprotease ADAM 19, have identified polymorphisms and a characterized tissue expression pattern, must have utility. The sequences of the present invention which encode variants of the human metalloprotease ADAM 19, which is well known to those of skill in the art and therefore provide specific markers for a human genome (see also chromosome mapping discussion below and information provided in the specification at page 3, lines 2-6 that indicate that this protein is encoded on human chromosome 5). Thus, those skilled in the art would instantly recognize that the sequences of the present invention would be an ideal, novel candidate for assessing gene expression using, for example, DNA chips, as the specification details. Accordingly, the present sequence has a specific utility in such DNA chip applications. Clearly, compositions that enhance the utility of such DNA chips, such as the presently claimed nucleotide sequence encoding variants of the human metalloprotease ADAM19, must also be useful. The Examiner is further requested to reconsider that, given the huge expense of the drug discovery process, even negative information obtained using these specific markers of expression of a variants of the human metalloprotease ADAM19, a protein of well-established activity provides very specific markers for the human genome and have great "real world" practical utility. Knowing that a given gene is not expressed in medically relevant tissue provides an informative finding of great value to industry by allowing for the more efficient deployment of expensive drug discovery resources. Such practical considerations are equally applicable to the scientific community in general, in that time and resources are not wasted chasing what are essentially scientific dead-ends (from the perspective of medical relevance). Clearly,

compositions that enhance the utility of DNA gene chips, such as the presently claimed sequences encoding variants of the human metalloprotease ADAM 19, must in themselves be useful. Moreover, the presently described human ADAM 19 sequences provide uniquely specific sequence resources for identifying and quantifying full length transcripts that were encoded by the corresponding human genomic locus. Accordingly, there can be no question that the described sequences provide an exquisitely specific utility for analyzing gene expression. Thus, the present claims clearly meet the requirements of 35 U.S.C. § 101.

Further evidence of utility of the presently claimed polynucleotide, although only one is needed to meet the requirements of 35 U.S.C. § 101 (*Raytheon v. Roper*, 220 USPQ 592 (Fed. Cir. 1983); *In re Gottlieb*, 140 USPQ 665 (CCPA 1964); *In re Malachowski*, 189 USPQ 432 (CCPA 1976); *Hoffman v. Klaus*, 9 USPQ2d 1657 (Bd. Pat. App. & Inter. 1988)), is the specific utility the present nucleotide sequence has in determining the genomic structure of the corresponding human chromosome, for example mapping the protein encoding regions as described in the specification. Clearly, the present polynucleotide provides exquisite specificity in localizing the specific region of human chromosome 5 that contains the gene encoding these variants of the human metalloprotease ADAM, a utility not shared by virtually any other nucleic acid sequence. In fact, it is this specificity that makes this particular sequence so useful. Early gene mapping techniques relied on methods such as Giemsa staining to identify regions of chromosomes. However, such techniques produced genetic maps with a resolution of only 5 to 10 megabases, far too low to be of much help in identifying specific genes involved in disease. The skilled artisan readily appreciates the significant benefit afforded by markers that map a specific locus of the human genome, such as the present nucleic acid sequence.

The Action discounts Applicants' assertion regarding the use of the presently claimed polynucleotides for gene mapping and determining chromosome structure again based on the position that such a use would allegedly be generic and therefore fail to represent a specific and substantial utility. However, as only a minor percentage of the genome actually encodes exons, which in turn encode amino acid sequences, the presently claimed polynucleotide sequence provides biologically validated empirical data (*e.g.*, showing which sequences are transcribed, spliced, and polyadenylated) that *specifically* defines that portion of the corresponding genomic locus that actually encodes exon sequence. Equally significant is that the claimed polynucleotide sequence defines how the encoded exons are actually spliced together to produce an active transcript (*i.e.*, the described sequences are

useful for functionally defining exon splice-junctions). The Applicants respectfully submit that the practical scientific value of expressed, spliced, and polyadenylated mRNA sequences is readily apparent to those skilled in the relevant biological and biochemical arts. For further evidence supporting the Applicants' position, the Board is requested to review, for example, section 3 of Venter *et al.* (*supra* at pp. 1317-1321, including Fig. 11 at pp.1324-1325), which demonstrates the significance of expressed sequence information in the structural analysis of genomic data. The presently claimed polynucleotide sequence defines a biologically validated sequence that provides a unique and specific resource for mapping the genome essentially as described in the Venter *et al.* article.

In addition to other uses, the mapping of the relatively few expressed human genes to a particular chromosome has long been a recognized method of identifying a genes associated with particular diseases. Furthermore, the mapping of the human chromosome is a project of such widely recognized importance by those of skill in the art and even lay people, that both the US government and private corporations have dedicated millions of dollars to such a project. One is thus forced to ask, if the mapping of human chromosomes is a throw away utility then why has the US government spent so many taxpayer dollars on this project?

The Action's repeated position that this utility, like the use of these specific sequences on DNA chips or the described polymorphisms in forensic analysis, is that since other molecules can be used to map the human chromosome or on DNA chips or in forensic analysis, these utilities are not specific or substantial. As described previously above, Applicants once again point out that these arguments are completely rebuffed by the Federal Circuit's holding in *Carl Zeiss, supra* ("[A]n invention need not be the best or only way to accomplish a certain result"). Furthermore, the argument that just because there are other objects having the same utility, that utility has been rendered generic and therefore invalid begs the question, previously presented, that don't all golf balls and tires have the same utility of other golf balls or tires, i.e. they can be used as golf balls or tires respectively and yet these items are readily considered to have patentable utility.

It has been clearly established that a statement of utility in a specification must be accepted absent reasons why one skilled in the art would have reason to doubt the objective truth of such statement. *In re Langer*, 503 F.2d 1380, 1391, 183 USPQ 288, 297 (CCPA, 1974; "*Langer*"); *In re Marzocchi*, 439 F.2d 220, 224, 169 USPQ 367, 370 (CCPA, 1971). As clearly set forth in *Langer*:

As a matter of Patent Office practice, a specification which contains a disclosure of utility which corresponds in scope to the subject matter sought to be patented must be taken as sufficient to satisfy the utility requirement of § 101 for the entire claimed subject matter unless there is a reason for one skilled in the art to question the objective truth of the statement of utility or its scope.

*Langer* at 297, emphasis in original. As set forth in the MPEP, “Office personnel must provide evidence sufficient to show that the statement of asserted utility would be considered ‘false’ by a person of ordinary skill in the art” (MPEP, Eighth Edition at 2100-40, emphasis added). Thus, the present claims clearly meet the requirements of 35 U.S.C. § 101.

Finally, with full recognition of the fact that all patent applications are examined on their own merits and that the prosecution of one patent does not effect the prosecution of another patent, *In re Wertheim*, 541 F.2d 257, 264, 191 USPQ 90, 97 (CCPA 1976), however the issue at hand in one of whether the fact that patents have issued recognizing the utility of a class of molecules does this confers a statutory precedent of patentability to a broad class of compositions. Thus, there remains a lingering issue regarding due process and equitable treatment under the law. While Applicants are well aware of the new Utility Guidelines set forth by the USPTO, Applicants respectfully point out that the current rules and regulations regarding the examination of patent applications is and always has been the patent laws as set forth in 35 U.S.C. and the patent rules as set forth in 37 C.F.R., not the Manual of Patent Examination Procedure or particular guidelines for patent examination set forth by the USPTO. Furthermore, it is the job of the judiciary, not the USPTO, to interpret these laws and rules. Applicants are unaware of any significant recent changes in either 35 U.S.C. § 101, or in the interpretation of 35 U.S.C. § 101 by the Supreme Court or the Federal Circuit that is in keeping with the new Utility Guidelines set forth by the USPTO. This is underscored by numerous patents that have been issued over the years that claim nucleic acid fragments that do not comply with the new Utility Guidelines. As examples of such issued U.S. Patents, the Examiner is invited to review U.S. Patent Nos. 5,817,479, 5,654,173, and 5,552,281 (each of which claims short polynucleotides; **Exhibits N-P**; copies of issued U.S. Patents not provided pursuant to current United States Patent and Trademark Office policy), and recently issued U.S. Patent No. 6,340,583 (which includes no working examples; **Exhibit Q**; copies of issued U.S. Patents not provided pursuant to current United States Patent and

Trademark Office policy), none of which contain examples of the “real-world” utilities that the Examiner appears to desire. As issued U.S. Patents are presumed to meet all of the requirements for patentability, including 35 U.S.C. §§ 101 and 112, first paragraph (see Section IV, below), Applicants submit that the present polynucleotides must also meet the requirements of 35 U.S.C. § 101. While Applicants agree that each application is examined on its own merits, Applicants are unaware of any changes to 35 U.S.C. § 101, or in the interpretation of 35 U.S.C. § 101 by the Supreme Court or the Federal Circuit, since the issuance of these patents that render the subject matter claimed in these patents, which is similar to the subject matter in question in the present application, as suddenly non-statutory or failing to meet the requirements of 35 U.S.C. § 101. Thus, holding Applicants invention to a different standard of utility appears inconsistent and inequitable, such a judgement being arbitrary and capricious, a violation of due process and equal protection under the law and cannot be maintained.

In summary, Applicants have described novel nucleic and amino acid sequences that encode variants of the human metalloprotease, ADAM 19, naturally occurring polymorphisms within these molecules and the tissue specific expression pattern of these variants. Furthermore, it is clear from the evidence provided that the sequences of the present invention encode variants of the human metalloprotease, ADAM 19, a protein of well recognized function. Thus, the present situation directly tracks Example 10 of the Revised Interim Utility Guidelines Training Materials (pages 53-55), which establishes that a rejection under 35 U.S.C. § 101 as allegedly lacking a patentable utility and under 35 U.S.C. § 112, first paragraph as allegedly unusable by the skilled artisan due to the alleged lack of patentable utility, is not proper when the invention encodes a protein that has a well known function. Still, further, this response has described a series of additional substantial, specific, credible and well-established utilities for the present invention. Therefore, Applicants submit that as the presently claimed sequence molecules have been shown to have a substantial, specific, credible and well-established utility, the rejection of the claims under 35 U.S.C. § 101 and under 35 U.S.C. § 112, first paragraph, should not have been made and Applicants respectfully request that the rejection be withdrawn.

#### **V. Rejection of Claims Under 35 U.S.C. § 112, First Paragraph**

The Action also rejects claims under 35 U.S.C. § 112, first paragraph, since allegedly one skilled in the art would not know how to use the invention, as the invention allegedly is not supported

by a specific, substantial, and credible utility or a well-established utility. Applicants respectfully traverse.

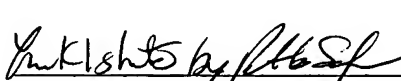
Applicants submit that as the present invention has been shown to have “a specific, substantial, and credible utility”, as detailed in the section above, the rejection under 35 U.S.C. § 112, first paragraph, should not have been made and Applicants therefore request that the rejection of the pending claims under 35 U.S.C. § 112, first paragraph, be withdrawn.

## **VI. Conclusion**

The present document is a full and complete response to the Action. In conclusion, Applicants submit that, in light of the foregoing remarks, the present case is in condition for allowance, and such favorable action is respectfully requested. Should Examiner Moore have any questions or comments, or believe that certain amendments of the claims might serve to improve their clarity, a telephone call to the undersigned Applicants' representative is earnestly solicited.

Respectfully submitted,

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Date

  
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